The TEDDY Working Group on Off Label Use in Paediatrics

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Off-label use in children

- Ranging from 40-90% depending on population and definitions

- Hence, more research is needed,
- BUT, in the meantime:

How do we prescribe effective and safe?

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Lack of label ≠ lack of evidence!

- **Off-label use = more adverse events**
- **? Should we restrict off-label use?**
- **Lack of label** ≠ lack of evidence!
- **Therefore: we need guidance!**

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Declaration on Good Off-Label Use Practice

- **Belgian initiative**
- **But: supported financially by lobby organization of industry**

- **Why?:** Recent concerning events in Member States following the passing of legislation to promote the off-label use of medicines for economic purposes, highlight the importance of preserving the European regulatory framework to ensure the safety of patients.

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Off-label Use of medicinal products should only occur if the following criteria are met:

1. Presence of a severe, life-impairing or life-threatening condition;
2. Absence of authorised treatment or repeated treatment failure;
3. Absence of alternative treatments authorised for the condition;
4. The off-label use is supported by strong evidence in scientific literature;
5. The patient has been educated and has given his or her informed consent;
6. Presence of established reporting routes for adverse events and linked to off-label use.

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Goal of Declaration

- Call on the European Medicines Agency to adopt strict guidelines to support healthcare practitioners and ensure economic benefit does not prevail over public health.

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NOT in best interest CHILDREN

ACTION:

TEDDY Working group GOLUP

Goal:

Declaration of Pediatric off-label prescribing
Convince EMA not to adopt Belgian Declaration

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GOLUP team

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Lucia Ruggeri (Italy)

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Helen Shaw (UK)

Mark Turner (UK)

Evelyne Jacqz-Aigrain (France)

Maria Mellado Pena (Spain)

Talia Sainz Costa (Spain)

Tjitske van der Zanden (the Netherlands)

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Action plan

1. Survey on regulations of off-label use in EU countries, including reimbursement

2. Write Pediatric Declaration/guideline for prescribing

3. Lobby EC/EMA/writers of Declaration

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Lobby activities

1. Lucia and Tjitske visited MEP meeting on the Declaration in EP, Fall 2016

    - Voiced our concerns

2. Follow-up: invitation by lobby group to visit Brussels

Tjitske and Saskia met with Dr Doome and lobby company

    - Again voiced our concerns, with examples
    - well received
    - will study possibility to adjust the Declaration

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Off label survery

Survey was developed

Audience: key leaders in pediatric pharmacology

Geography: Europe

Main questions

- How is off-label prescribing regulated?
- How relates off-label prescribing to reimbursement?

Status:

Not sent, as a European survey, not specific for children is being undertaken. Results?

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Off label statement for children

To contain framework for off-label prescribing in children

We have started a draft for the Declaration

Discussion points:

Do we need a pediatric specific Declaration?
Do we wait for Doome et al to adjust their Declaration?

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Framework proposal – step 1

Is there licensed alternative? No, then:

Is drug advised in official treatment guidelines? No, then:

Is there sufficient scientific literature supporting effective and safe use?, No, then:

Is there sufficient practical experience with use of drug? No, then:

Make a ‘individualized’ efficacy and safety evaluation.

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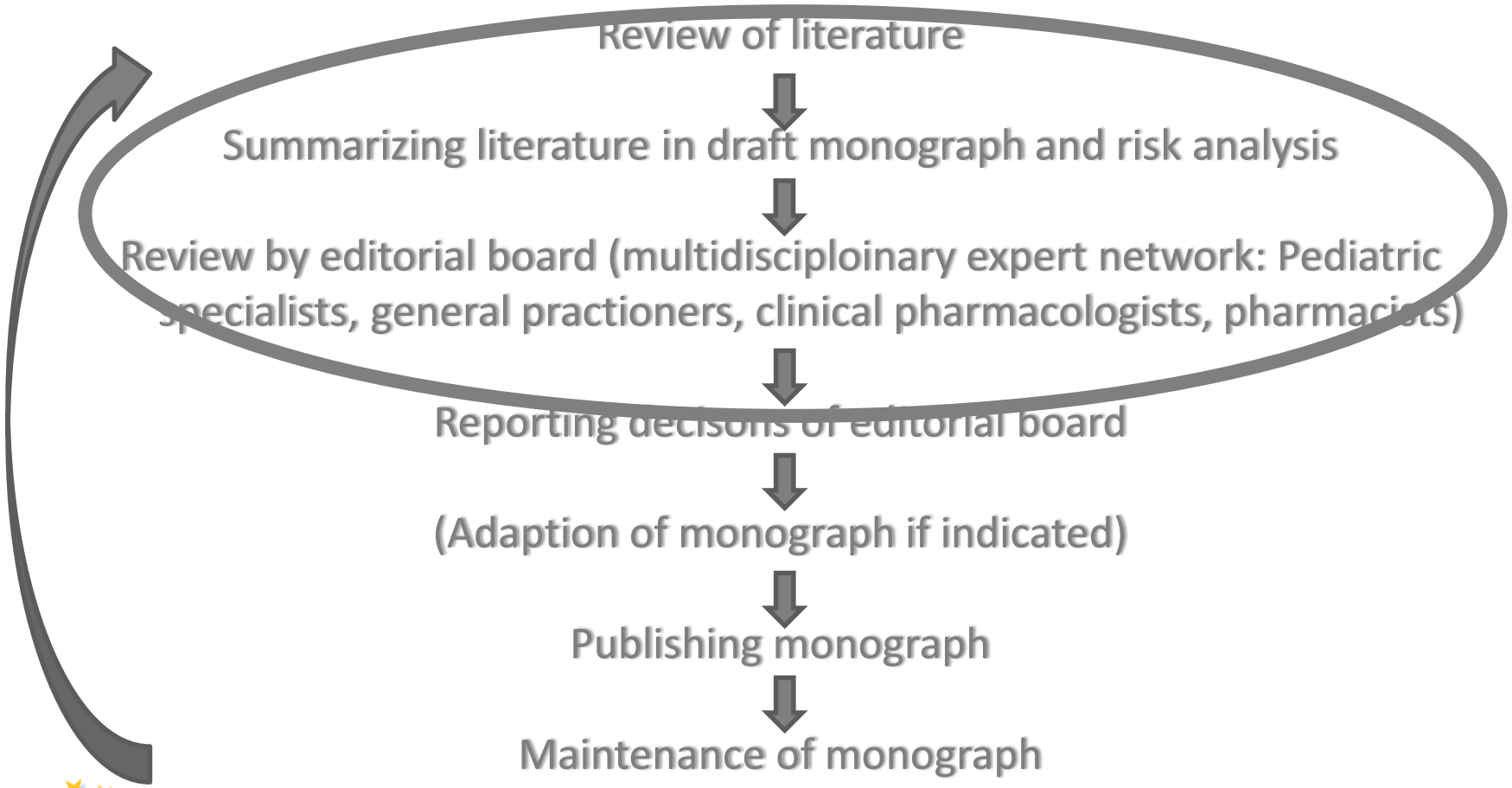
Kinderformularium

Life cycle of a drug monograph



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Framework proposal – Step 2

Perform a ‘individualized’ efficacy and safety evaluation,

Including

- Does the mechanism support intended therapeutic use?
- Are there specific safety concerns?
- Is the PK_PD relationship to be similar as in registered use?
- PK known in age of patient?
- Can PK be extrapolated?
- Is a suitable formulation available?
- Are their specific ethical questions?

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Framework proposal – Step 3

Start treatment

- For drugs where individualized evaluation is done:

- Document detailed outcome of evaluation in medical chart
- Discuss off-label use with parents
- Report any safety issues with the pharmacovigilance center
- Preferably: report in prospective registries

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Thank you!

Any questions?

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